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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,529	05/10/2002	Achim Berthold	512100-2025	6199

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,529	BERTHOLD ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

James M. Spear
JAMES H. [illegible]
[illegible]
AU 1615

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' amendment, filed 07/14/2004.

Claims 1-12 have been canceled, and claims 13-23 have been added and included in the prosecution.

Claim Rejections - 35 USC § 103

1. Claims 13-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,983,395 ('395) in view of US 4,879,119 ('119).

US '395 discloses a transdermal drug delivery device comprising a drug formulation containing reservoir defined by a backing layer and a drug permeable membrane layer, and a peelable release liner (abstract; col.2, lines 30-57). The reservoir comprises ethanol, enhancer, and nicardipine (col.7, lines 55-60). The reference disclosed nifedipine as one of the dihydropyridines that are suitable to be included in the reservoir (col.5, line 25).

The reference does not teach the pyrrolidone derivatives, sorbitan palmitate as specific enhancers, or lacipidine species of dihydropyridines. The reference does not teach specific amounts of different ingredients as claimed.

It is within the skill in the art to replace one species by another known to perform the same function. Thus, claiming lacipidine does not render the claim patentable, absent evidence to the contrary.

The amounts of different ingredients do not impart patentability to the claims, absent evidence to the contrary.

US '119 teaches a skin patch having good transdermal properties showing increased skin penetration rate of the drug and an increased drug releasing rate (abstract; col.1, lines 9-12). The good transdermal properties are provided by a patch comprising a solution comprising the drug and penetration enhancer, such as sorbitan middle chain fatty acid ester (abstract; col.3, lines13-15). Drugs suitable for delivery by those patches are nicardipine and nifedipine dissolved in ethanol, N-methyl-2-pyrrolidone or mixture thereof (col.2, lines 33-34; col.49-58).

Thus, it would have been obvious to one having ordinary skill in the art a the time of the invention to provide a transdermal patch comprising reservoir comprising dihydropyridine, ethanol, and penetration enhancer as disclosed by US '395, and add the pyrrolidone derivative and the select sorbitan ester as an enhancer as disclosed by US '119, motivated by the teaching of US '119 that a patch with such ingredients has good transdermal properties showing increased skin penetration rate of the drug and an increased drug releasing rate, with reasonable expectation of having a transdermal drug delivery device to deliver dihydropyridine in a reservoir comprising ethanol, pyrrolidone derivative and sorbitan ester that deliver the drug to the patient in need with great success.

2. Claims 13-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,045,553 (553) in view of US '119.

US '553 teaches a pharmaceutical composition for percutaneous drug absorption comprising dihydropyridine compound to treat hypertension and angiopathy (abstract; col.1, lines 34-37). The composition is included in a patch comprising a support member, drug-containing layer, and release controlling membrane (col.2, lines 35-40; figures 1-6; col.4, line 12). The composition comprising nilvadipine in an amount of 5% by weight, unsaturated fatty acid, and pyrrolidone derivative (col.2, lines 45-61; col.4, lines 49-50; examples).

The reference does not teach the specific pyrrolidone derivatives, sorbitan palmitate as specific enhancers, or lacipidine and nifedipine species of dihydropyridines. The reference does not teach specific amounts of different ingredients as claimed.

It is within the skill in the art to replace one species by another known to perform the same function. Thus, claiming lacipidine or nifedipine does not render the claim patentable, absent evidence to the contrary.

The amounts of different ingredients do not impart patentability to the claims, absent evidence to the contrary.

US '119 teaches a skin patch having good transdermal properties showing increased skin penetration rate of the drug and an increased drug releasing rate (abstract; col.1, lines 9-12). The good transdermal properties are provided by a patch comprising a solution comprising the drug and penetration enhancer, such as sorbitan

middle chain fatty acid ester (abstract; col.3, lines13-15). Drugs suitable for delivery by those patches are nicardipine and nifedipine dissolved in ethanol, N-methyl-2-pyrrolidone or mixture thereof (col.2, lines 33-34; col.49-58).

Thus, it would have been obvious to one having ordinary skill in the art a the time of the invention to provide a transdermal patch comprising reservoir comprising dihydropyridine, ethanol, and penetration enhancer as disclosed by US '553, and select sorbitan ester as an enhancer as disclosed by US '119, motivated by the teaching of US '119 that a patch with such ingredients has good transdermal properties showing increased skin penetration rate of the drug and an increased drug releasing rate, with reasonable expectation of having a transdermal drug delivery device to deliver dihydropyridine in a reservoir comprising ethanol, pyrrolidone derivative and sorbitan ester that deliver the drug to the patient in need with great success.

3. Claims 13-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 680 759 ('759) in view of US '119.

EP '759 teaches a transdermal delivery of calcium channel blockers, such as nifedipine to treat angina and hypertension (abstract; page 2, lines 50-53). The device comprises a backing layer, a reservoir containing the drug, and a semi-porous membrane (page 6, lines 15-28; page 8, lines 10-14). The reservoir comprises the drug, ethanol, and permeation enhancer (abstract; page 7, lines 39-55).

The reference does not teach the pyrrolidone derivatives, sorbitan palmitate as specific enhancers, or lacipidine species of dihydropyridines. The reference does not teach specific amounts of different ingredients as claimed.

It is within the skill in the art to replace one species by another known to perform the same function. Thus, claiming lacipidine does not render the claim patentable, absent evidence to the contrary.

The amounts of different ingredients do not impart patentability to the claims, absent evidence to the contrary.

US '119 teaches a skin patch having good transdermal properties showing increased skin penetration rate of the drug and an increased drug releasing rate (abstract; col.1, lines 9-12). The good transdermal properties are provided by a patch comprising a solution comprising the drug and penetration enhancer, such as sorbitan middle chain fatty acid ester (abstract; col.3, lines13-15). Drugs suitable for delivery by those patches are nicardipine and nifedipine dissolved in ethanol, N-methyl-2-pyrrolidone or mixture thereof (col.2, lines 33-34; col.49-58).

Thus, it would have been obvious to one having ordinary skill in the art a the time of the invention to provide a transdermal patch comprising reservoir comprising dihydropyridine, ethanol, and penetration enhancer as disclosed by EP '759, and add the pyrrolidone derivative and the select sorbitan ester as an enhancer as disclosed by US '119, motivated by the teaching of US '119 that a patch with such ingredients has good transdermal properties showing increased skin penetration rate of the drug and an increased drug releasing rate, with reasonable expectation of having a transdermal drug

delivery device to deliver dihydropyridine in a reservoir comprising ethanol, pyrrolidone derivative and sorbitan ester that deliver the drug to the patient in need with great success.

Response to Arguments

4. Applicant's arguments filed 07/14/2004 have been fully considered but they are not persuasive.

Applicants traverse the 35 U.S.C. rejections of the claims by arguing that US '395 teaches a gel, US '553 teaches a suspension, and EP'759 teaches dispersion, and none of the references teaches a solution. US '119 teaches the drug dispersed in a solid base and not solution. US '119 teaches the use of N-methyl-2-pyrrolidone as a solvent and not as an enhancer and does not provide motivation to add it as penetration enhancer. Combination of any of US '395, US '553 or EP '759 and US '119 would not result in a solution.

In response to the above applicants' arguments, the examiner position is that the claims are directed to a product, and all the elements of the products are taught by the references in combination. The art recognized the need to have the calcium antagonist of the dihydropyridine type in the soluble form to increase its transdermal delivery. Therefore, different solvent such ethanol or others used to dissolve the drugs into as applicants did. US '119 used N-methyl-2-pyrrolidone to dissolve the drugs for the same purpose desired by applicants, i.e. increase skin penetration and drug release rate. All the references disclosed the use of the ethanol as applicants did. The expression

"comprising" of the claim language does not exclude the presence of other ingredients, such as gelling agents, or fatty acids other than those claimed by applicants. One having ordinary skill in the art would have expected to achieve a reservoir comprising the same ingredients claimed by applicants and the reservoir would have been expected to be in the form of solution as it results from combining elements that all dissolve the drug. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify or combine the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972). A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). As stated in *In re Kerkhoven,* 205 USPQ 1069, 1072 (CCPA 1980), "It is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third

composition which is to be used for the very same purpose". As the court explained in *In re Crockett,* 126 USPQ 186, 188 (CCPA-1990), the idea of combining the two compositions flows logically from their having been individually taught in the prior art. Therefore, the invention as whole would have been *prima facie* obvious to one of ordinary skill in the art.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

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